The Pediatric Stroke Code: Early Management of the Child with Stroke

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Stroke in children is estimated to occur as frequently as brain tumors, and acute presentations should be considered a neurologic emergency. Although stroke is less common in children than in adults, the long-term morbidity and societal impact of stroke in children likely exceeds that in adults.[1] Lessons from adult stroke trials underscore the need for early therapy to prevent complications and improve outcomes. In children, the prompt diagnosis of stroke is challenging, and a delay in diagnosis is a major impediment to initiating therapy.[2,3] Subspecialty services required for emergent diagnosis and management of pediatric stroke are available at most academic medical centers.

Although guidelines for the management of stroke in children exist,[4] care varies by institution, and interventions to minimize morbidity and prevent complications are often applied inconsistently. Herein we propose the "pediatric stroke code," a systematic, multidisciplinary approach to early management of the child with stroke, including hospital preparedness, timely diagnosis, hyperacute therapy, supportive care, management of complications, and secondary stroke prevention. The recommendations discussed are for children and are not applicable to neonates. Neonatal stroke is differentiated from childhood stroke based on differences in etiology, risk factors, and presentation.

Adult Stroke Care Delivery: What Have We Learned?

Dedicated stroke care and comprehensive stroke units provide standardized, multidisciplinary care for adults. This model of care improves acute and long-term outcomes regardless of patient age, sex, stroke severity, or the use or nonuse of tissue plasminogen activator (tPA).[5-10] These improved outcomes are attributed to a comprehensive multidisciplinary approach; specialization of medical, nursing, and rehabilitation staff; early access to rehabilitation; and education for patients and their families.[6,11]

CT	Computed tomography
DSA	Digital subtraction angiography
DWI	Diffusion-weighted imaging
IAT	Intra-arterial thrombolysis
IV	Intravenous
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
SCD	Sickle cell disease
TOF	Time-of-flight
tPA	Tissue plasminogen activator
TTE	Transthoracic echocardiography

Although dedicated stroke units might not be a viable option for pediatric hospitals, extrapolation from the impact of stroke centers on outcomes in adults suggests important opportunities for advancing acute care for children with stroke. Such measures include standardized implementation of best-practice guidelines and multidisciplinary patient care. The precedent from a comparable approach to severe pediatric traumatic brain injury suggests that this team-based management of stroke is feasible and may significantly improve outcomes.[12]

Education and Stroke Recognition

The median time from presentation to diagnosis of stroke in children is almost 24 hours, with in-hospital delays accounting for the largest proportion of this time.[2] Delayed recognition of stroke in childhood has been associated with stuttering onset of symptoms, altered level of consciousness, and lack of initial neuroimaging at a tertiary hospital.[2,13,14] Fluctuating deficits consistent with transient ischemic attacks may herald an arteriopathy, one of the most common causes of childhood stroke.[15] Delayed diagnosis also may occur in patients presenting with nonspecific symptoms, such as headache, seizures, ataxia, or difficulty with fine-finger movements, because these are more commonly associated with migraine, infection, seizure, and conversion disorder.

Early recognition of ischemic stroke may be facilitated by the use of screening protocols in the emergency department for signs and symptoms of stroke, which may include acute onset of hemiparesis, aphasia, hemisensory loss, change in vision, and loss of balance. Age-modified stroke recognition tools have been proposed, but require further development and validation.[16] Certain underlying conditions, including heart disease, sickle cell disease (SCD), infections, malignancy, use of oral contraceptives, inflammatory/autoimmune diseases, and head and neck trauma, should increase the suspicion for stroke in a child. Collaboration with the emergency department and nursing personnel is an essential step in developing the infrastructure for screening a child for stroke. Once a child with possible stroke is identified, neurology and critical care specialists should be consulted, and neuroimaging initiated.

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Baseline Assessment

Neurologic Exam

Establishing a baseline neurologic deficit is critical for initial assessment and monitoring. The pediatric version of the National Institutes of Health Stroke Scale has been validated for use by trained child neurologists in children aged 2-17 years.[17,18] Any deterioration in clinical examination findings after admission warrants urgent neuroimaging to rule out malignant cerebral edema, hemorrhagic conversion, or recurrent stroke.

Diagnostic Laboratory Studies

Baseline laboratory studies are listed in Figure 1 (available at www.jpeds.com). In a child being treated with chronic anticoagulation, studies to assess therapeutic range are indicated. A type-and-screen should be ordered for children at high risk for intracranial hemorrhage and for all children before treatment with tPA.

Cardiac Evaluation

Because congenital and acquired heart disease is a common cause of stroke in children, transthoracic echocardiography (TTE) is indicated in all children with stroke. TTE should be performed promptly after the diagnosis of stroke to evaluate for a cardiac thrombus, vegetation, or right-to-left shunt. A "bubble" or "contrast" study is indicated in children with recurrent strokes of unknown etiology to assess for patent foramen ovale or pulmonary arteriovenous malformation.[19] In rare cases, transesophageal echocardiography may detect abnormalities not seen on TTE, particularly vegetations and left atrial thrombi.[20] In addition, electrocardiography should be performed to rule out arrhythmias.

Neuroimaging

The experience of adult stroke centers highlights the importance of timely neuroimaging to establish the diagnosis of stroke and rule out intracranial hemorrhage.[11] Designation as an adult primary stroke center requires the ability to perform computed tomography (CT) of the head within 25 minutes and the availability of this imaging modality 24 hours a day, 7 days a week. The high frequency of stroke mimics in children makes confirmation of stroke especially important.[3,21] A CT scan will often miss early signs of ischemic infarction and thus is not sufficient for ruling out stroke in a child. Magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI), along with magnetic resonance angiography (MRA) of the head and neck, should be performed in all children with suspected acute ischemic stroke. Stroke neuroimaging protocol may include axial T2 fluid-attenuated inversion recovery, susceptibility-weighted imaging or gradient echo, and DWI/apparent diffusion coefficient MRI and time-of-flight (TOF) MRA of the head and neck. In many centers, these sequences can be performed in 20-25 minutes. The initial MRI also may be a limited protocol with DWI and susceptibility-weighted imaging/gradient echo sequences to quickly establish the presence of ischemia and hemorrhage. Some centers do not have MRI capability 24 hours a day, 7 days a week; in these instances, head CT to rule out hemorrhage, admission for observation and neuroprotection, and treatment with aspirin may be indicated until MRI can be performed.

If an arterial abnormality is suspected on TOF MRA, more specific angiography may be required to better define the arterial lesion and assess for additional lesions in the distal circulation. This can be performed with contrast imaging using MRA, MRI high-resolution arterial wall imaging, CT angiography, or digital subtraction angiography (DSA).[22] Although DSA is considered the gold standard for arterial imaging, it is invasive and can be technically challenging in small children.[23] CT angiography is more widely available than DSA and provides greater luminal detail than TOF MRA for characterizing arterial lesions, such as dissection, vasculitis, and moyamoya disease. The risk of radiation exposure associated with both CT and digital subtraction angiography must be weighed against the likelihood of finding an additional abnormality that would alter management or prognosis.

In adults, transcranial Doppler may be useful for characterizing flow abnormalities on MRA, detecting circulating microemboli in patients with potential embolic sources including dissection, and monitoring for vasospasm in patients with subarachnoid hemorrhage. In children, it is most frequently used for stroke risk stratification in patients with SCD.[24]

Hyperacute Therapy

Intravenous Thrombolysis

In adults, intravenous (IV) tPA has been approved by the Food and Drug Administration for use within 3 hours of stroke onset, and a recent American Heart Association/American Stroke Association advisory recommends extending this time window to 4.5 hours.[7] When administered within 4.5 hours for arterial ischemic stroke, IV tPA is associated with symptomatic intracranial hemorrhage in 2.6% of adults.[25] A recent study of thrombolysis in young adults (aged 16-49 years) showed that these patients benefited from IV tPA and may be at lower risk for symptomatic intracranial hemorrhage compared with older adults.[26]

There are multiple published case reports of children receiving IV tPA for acute stroke, almost all of which report tPA administered following established safety guidelines with good outcomes[27-39]; however, other studies have reported significant deviations from adult stroke thrombolysis guidelines with delayed use of tPA and variable dosing, illustrating the need for safety data in children.[40] Given the absence of safety data and the high rate of stroke mimics in children, tPA should be considered only in select patients presenting with a significant, persistent neurologic deficit with evidence of ischemic infarction and arterial occlusion on neuroimaging.[41] Treatment contraindications and dosing should follow established safety guidelines for adults. Before